Appln No.: 09/601,644
Amendment Dated: October 11, 2004
Reply to Office Action of August 10, 2004

REMARKS/ARGUMENTS

This is in response to the Office Action mailed August 10, 2004 for the above-captioned application. In response to the restriction requirement set forth in the Office Action, Applicants hereby elect the invention of Group I, and Shiga-like toxin as both the heteromeric toxin and the binding subunit. For screening cells, Applicants elect tumor cells. This election is made **with traverse**, based on the amendments to the claims and the arguments as set forth below.

Claims 1 and 32 have been amended after consideration of the Examiner's remarks concerning the phrase "substantially insensitive" and this amendment is discussed further below. Claim 24 is amended to correct a typographic error. Claim 42 has been added dependent on claim 1 to refer to the specific instance in which the screening cells are insensitive to the wild-type toxin.

Of the elected Group, claims 1, 2, and 5-16 are generic with respect to the elected invention. Claims 3 and 4 are drawn to non-elected species.

With respect to the amendment to the claims, and the restriction requirement in general, an important difference between the references cited by the Examiner and the invention, which was embodied in the term "substantially insensitive" in the original claims, is the fact that in the art cells are used that are generally sensitive to the wild type toxin, and less sensitive to the mutants. In contrast, for purposes of the present invention cells that have a lower sensitivity, or even no sensitivity to the wild type toxin such that toxins are selected that have greater toxicity than the wild-type toxin relative to these cells. Because of the difficulty in expressing this concept without reliance on unacceptable relative terminology, Applicants have amended claims 1 and 32 to state just a population of screening cells and that the selected protein is one that kills or inhibits that population of screening cells **to a greater extent than the wild-type cytotoxic protein.** It will be understood that the original requirement of limited sensitivity to the wild type protein is also reflected in this limitation, since otherwise it would be impossible to distinguish between clones producing (1) a protein in which no mutation had occurred, (2) a protein in which an irrelevant mutation had occurred; and (3) a protein in which a significant mutation had occurred to produce a different toxic protein. The present invention is concerned with the latter type of protein, and so only screening cells where an increase in toxicity can be observed are suitable.

As noted above, this is different from the art cited by the Examiner, in which sensitive cells are used and a reduction in toxicity is looked for. This difference makes the lack of unity argument inappropriate. Furthermore, it highlights the fundamental difference between the references which were interested in the mechanism of action of a known toxin, and the present invention which is concerned with development of new toxins with difference types of activity.

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The amendment as now presented is supported throughout the application as filed. In particular, Applicants direct the Examiner's attention to Page 7, lines 13-16, in which a target cell (the screening population) is used "which is lacking or has lower levels of receptors which cause sensitivity to the wild type protein." Cells which have lower levels of receptors will not be as sensitive to the wild type protein, and so can be more sensitive to the mutant protein.

In view of the amendment, Applicants submit that the references relied upon in support of the lack of unity argument do not disclose the unifying feature of the claims. Accordingly, withdrawal of the restriction requirement and consideration of all claims are respectfully urged.

Respectfully Submitted,

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